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(54) Intraocular lens and dye therefor

(57) A yellow dye is capable of chemical bonding to a silicone which is a material of an intraocular lens or capable of copolymerizing with a radical polymerizable monomer which is a material of an intraocular lens. Such a dye is useful for providing lenses for eyes, having vis-

ible light transmission properties near to those of human crystalline lenses, and may be particularly effective for soft lenses for eyes.

EP 1 293 541 A2

EP 1 293 541 A2

Description

[0001] The present invention relates to synthesis of a dye and use thereof in an intraocular lens.

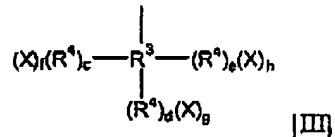
5 [0002] Lately, Influences of blue violet light on the human body have been reported. As a result of these influences, injuries to eyes, particularly light harm to the retina, are feared. Intraocular lenses which are inserted in eyes after an operation for cataract, contact lenses, implants of the cornea and other intraocular lenses should have a function of guarding against rays having such high energy. The sun emits ultraviolet, visible rays and infrared in large quantities. The sun emission, which arrives on the surface of the earth through the atmosphere, constitutes UV-B (230-300nm), near ultraviolet or UV-A (300-400nm), visible rays (400-700nm) and near infrared rays (700-1400nm). The human choroid mostly transmits near infrared rays and visible spectrum under common conditions. However, the cornea mostly absorbs UV-B so that the UV-B cannot reach the retina.

10 [0003] Senility changes of the transmission properties of ultraviolet and visible rays appear in human crystalline lenses by aging. The crystalline lenses freely transmit ultraviolet and visible rays in infancy, transmit the rays less with age, and become yellowish gradually. Particularly, as the transmissivity of rays between 400nm and 500nm slowly lower, the visible view becomes yellowish. The visual function then becomes used to such conditions. For this reason, 15 when the crystalline lenses of aged cataract patients are cut out and transparent artificial lenses are inserted into the eyes, the protective reactions of eyes, especially tissues of the retina and the like in fundus oculi, to protect from ultraviolet and near ultraviolet rays are lowered. As a result, the patient senses a bluish view after the surgical operation. It is called Chromatopsia.

20 [0004] In recent years, lenses for eyes to protect from harmful ultraviolet, particularly intraocular lenses, have become commercially available. These lenses are produced by mixing or chemical bonding of an ultraviolet absorber, which cuts off lights of less than 400nm, with a lens material, to lower the amount of incident ultraviolet to the eyes and protect the eyes from the harmful ultraviolet. Further, coloured intraocular lenses are available commercially. These lenses are produced by mixing or copolymerizing an ultraviolet absorber and a dye, which has absorption at a visible short 25 wave range, with a material of hard lenses. On the other hand, as the materials of intraocular lenses other than those of hard lenses, lenses produced by soft materials such as silicone elastomers and acrylic elastomers can be obtained commercially. When a dye is directly mixed or dispersed into these soft materials, there is a possibility of bleeding out of the dye because of high molecular motion of the materials themselves. Accordingly, in the case of production of coloured lenses with soft materials, the coloured molecules should be rigidly bonded to the polymer of the materials.

30 [0005] Japanese Patent Laid-open Publication H01-299560 discloses a material for an intraocular lens characterised by a polymerizable ultraviolet absorber having polymerizable groups selected from the groups comprising of acryloyl, methacryloyl, vinyl, allyl and isopropenyl and a polymerizable dye having polymerizable groups selected from the groups comprising of acryloyl, allyl and isopropenyl, which copolymerizes with another polymerizable monomer ingredient for lens production. Japanese Patent Laid-open Publication H02-503997 discloses a polymer lens material for 35 eyes, which contains one or more monomers for forming lenses selected from the groups comprising of acrylate monomers and methacrylate monomers and one or more polymerizable yellow dyes having one to four polymerizable acrylate or methacrylate groups, wherein the dye part is substituted for each acrylate or methacrylate group by a spacer group of the following formula [III].

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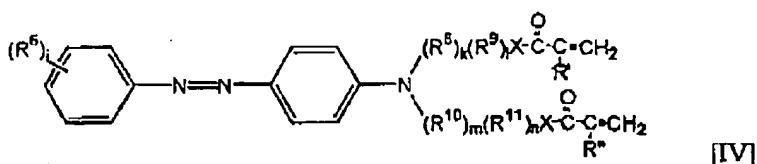
wherein R^3 is alkyl of less than 6 carbons; R^4 is a noncyclic organic spacer of less than ten atoms of C, H, Si, O, N, P, S, Cl, Br or F or a combination thereof; X is O, NH or NR^5 , wherein R^5 is alkyl of C_1-C_{10} ; d, e, g and h are independently integers in the range 0-4; and c and f are independently integers in the range 1-4.

50 [0006] Further, Japanese Patent Laid-open Publication H09-187500 discloses diacrylates/dimethacrylates of the following formula [IV].

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EP 1 293 541 A2

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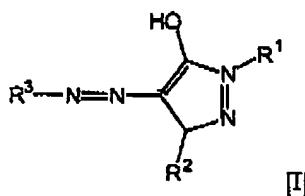
10 wherein R¹ and R² are independently H or CH₃, R⁶ and R⁷ are independently hydrogen, alkyl of C₁-C₂₀, OCH₃, OC₂H₅, OC₃H₇, or OC₄H₉, i and j are independently integers of 1 or 2, R⁸, R⁹, R¹⁰ and R¹¹ are independently noncyclic organic spacer groups of less than 10 atoms, the spacer groups being C, H, Si, O, N, P, S, Cl, Br or F or combinations thereof, k and m are independently integers in the range 1-6, 1 and n are independently integers in the range 0-6, and X is O, NH or NR⁵, wherein R⁵ is alkyl of C₁-C₁₀.

15 [0007] These techniques disclosed in known references apply a method for copolymerizing a polymerizable colouring agent or an ultraviolet absorbing agent with an acrylic or methacrylic polymer by radical polymerization. Materials of the coloured intraocular lenses produced by these techniques are hard polymethylmethacrylate. Although the above known techniques take effect to provide stable hard lenses, there are many problems because a suitable method for colouring soft intraocular lenses and a technique there for are not disclosed. Moreover, since azo dyes generally inhibit radical polymerization, the possibility remains of unpolymerized monomers or low molecular ingredients in polymer products. Some claims of these patent applications disclose dyes having a phenolic hydroxyl group. However, since the phenolic hydroxyl group traps growth radicals in the polymerization, it is not suited for radical polymerization. Some claims of these patent applications disclose dyes using an allyl group as a polymerizable group. The allyl group is poor in radical polymerization and unsuitable for such polymerization. Monomers having acryl or methacryl groups have high reactivity and high toxicity, so that these are difficult to treat.

20 [0008] Preferred embodiments of the present invention aim to provide lenses for eyes having visible light transmission properties near to those of human crystalline lenses, and particularly colouring techniques effective for soft lenses for eyes.

25 [0009] According to one aspect of the present invention, there is provided a dye for an intraocular lens having the following formula [I] or [II]:

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wherein R¹ is linear or branched alkyl of C₁-C₁₀ or phenyl; when R¹ is phenyl, one or more hydrogens of its aromatic ring may be substituted by linear or branched alkyl of C₁-C₁₀, linear or branched alkoxy of C₁-C₁₀, hydroxy, amino, sulfo, nitro, halogen, carboxy, -C(=O)-O-R⁴ or -C(=O)-NH-R⁴, wherein R⁴ is linear or branched alkyl of C₁-C₁₀.

45 R² is linear or branched alkyl of C₁-C₁₀, amino or phenyl; when R² is amino, one or both hydrogens thereof may be substituted by linear or branched alkyl of C₁-C₁₀; or when R² is phenyl, one or more hydrogens of its aromatic ring may be substituted by linear or branched alkyl of C₁-C₁₀, linear or branched alkoxy of C₁-C₁₀, hydroxy, amino, sulfo, nitro, halogen, carboxy, -C(=O)-O-R⁴, -C(=O)-NH-R⁴, wherein R⁴ is linear or branched alkyl of C₁-C₁₀.

50 R³ is phenyl or naphthyl, one or more hydrogens thereof are linear or branched alkyl of C₁-C₁₀, Linear or branched alkoxy of C₁-C₁₀, hydroxy, amino, sulfo, nitro, halogen, carboxy, -C(=O)-O-R⁴, -C(=O)-NH-R⁴, wherein R⁴ is linear or branched alkyl of C₁-C₁₀; and

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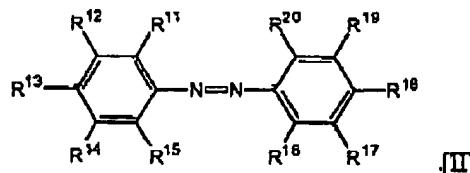
55 In formula [I], at least one hydrogen of the aromatic ring constituted in R¹, R² or R³ is substituted by any of CH₂CH₂, (CH₂)_m, CH₂=CH-(CH₂)_m-X¹-(CH₂)_n, CH₂=C(R⁵)-(CH₂)_m-X¹-C(=O)-(CH₂)_n, CH₂=C(R⁵)-(CH₂)_m-C(=O)-X¹-(CH₂)_n, (CH₂=C(R⁵)-(CH₂)_m)₂N-(CH₂)_n, or (CH₂=C(R⁵)-(CH₂)_m)₂N-C(=O)-(CH₂)_n; wherein X¹ is -O- or

EP 1 293 541 A2

-NR⁶, R⁵ and R⁶ are independently hydrogen, or linear or branched alkyl of C₁~C₁₀, and m and n are independently integers in the range 0 to 10:

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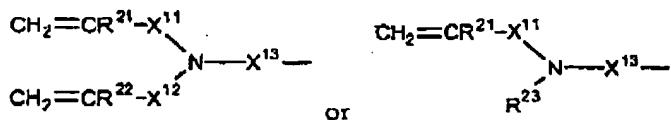
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wherein R¹¹, R¹², R¹³, R¹⁴, R¹⁵, R¹⁶, R¹⁷, R¹⁸, R¹⁹, and R²⁰ are independently selected from hydrogen, hydroxy, halogen, or linear or branched alkyl of C₁~C₁₀, and at least one of them is a substituted group represented by:

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wherein R²¹ and R²² are independently hydrogen or methyl, R²³ is hydrogen or linear or branched alkyl of C₁~C₁₀, X¹¹, X¹² and X¹³, independently, have covalent bonds, or linear or branched bivalent spacer groups, or -(CH₂)^m-O-(CH₂)ⁿ-O- where m and n are independently integers in the range 0 to 10.

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[0010] The invention extends to a colouring silicone material which is obtained from chemical bonding of the dye represented by formula [I] or [II] to a silicone polymer having hydrosilyl groups.

[0011] The invention extends to a colouring silicone material which is obtained from chemical bonding of the dye represented by formula [I] or [II] and an ultraviolet absorber having functional groups capable of chemical bonding to a silicone having hydrosilyl groups.

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[0012] In such a colouring silicone material, the silicone having hydrosilyl groups may be selected from the group comprising a dimethylsiloxane-methylhydrosiloxane copolymer, a diphenylsiloxane-phenylhydrosiloxane copolymer, polyethylhydrosiloxane, a methylhydrosiloxane-phenylmethylsiloxane copolymer, a methylhydrosiloxane-octylmethylsiloxane copolymer, a silicone resin containing hydrosilyl groups and polyphenyl(dimethylhydrosiloxyl)siloxane.

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[0013] The Invention extends to a silicone elastomer obtained by crosslinking of a silicone having hydrosilyl groups as above with a silicone having vinyl groups.

[0014] The Invention extends to a silicone elastomer obtained by crosslinking of a silicone having hydrosilyl groups as above with a silicone having vinyl groups and a silica.

[0015] The Invention extends to an intraocular lens comprising a dye, colouring silicone material or silicone elastomer as in any of the preceding aspects of the invention.

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[0016] A yellow dye according to a preferred embodiment of the present invention has a constitution able to bond chemically to transparent silicone having hydrosilyl groups by an addition reaction. Since the dye is able to attach directly to polymer chains, it has a much lower tendency to exude from materials after shaping for use in the eyes. As a yellow dye according to a preferred embodiment of the present invention has also radical polymerizability, it is possible to obtain coloured intraocular lenses by copolymerization with monomers of radical polymerizability such as acrylic and styrene types. More preferably, lens materials are obtained by using a method other than radical polymerization, namely by bonding the dye to a polymer chain. Yellow dyes according to preferred embodiments of the present invention may have a maximum absorption of 350-450nm. Lenses for eyes, obtained by bonding both the yellow dye and another ultraviolet absorbing agent to silicone or by copolymerization of the dye with a monomer constituting lenses, can shut off the greater part (more than 99%) of incident violet light to the eyes and lower blue light intensity to reduce the bad influence of light upon eyes. The lenses can be used as intraocular lenses, glasses, contact lenses and other lenses for eyes.

[0017] Coloured silicone obtained in a preferred embodiment of the present invention has its absorption band in the blue region. The silicone does not exude dye, and is suitable for use in contact with living organisms, and for long-term

EP 1 293 541 A2

use in the eyes.

[0018] For a better understanding of the invention, and to show how embodiments of the same may be carried into effect, examples thereof will now be described, and reference will be made, by way of example, to the accompanying diagrammatic drawings, in which:

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Figure 1 shows a transmission spectrum of ultraviolet-visible light of a plate sample of silicone elastomer in Example 1 described below; and

Figure 2 shows a transmission spectrum of ultraviolet-visible light of a plate sample of silicone elastomer in Example 3 described below.

[0019] An example of a yellow dye according to an embodiment of the present invention, which has the possibility of addition bonding to silicone, has a basic skeleton of azobenzene or phenylazopyrazolone, and it has unsaturated alkyl groups such as vinyl and allyl, to give the possibility of addition bonding to silicone polymers. Moreover, it has characteristics of blocking violet light and protection of eyes from not only blue light but also violet light by using a supporting mixture of the dye and an ultraviolet absorbing agent having the possibility of addition bonding to silicone at the same time, or by using a mixture of the dye and silicone supporting an ultraviolet absorbing agent.

[0020] A form of such a yellow dye is represented by a constitution of an enol type of the above general formula [I], and also by a keto type of the formula.

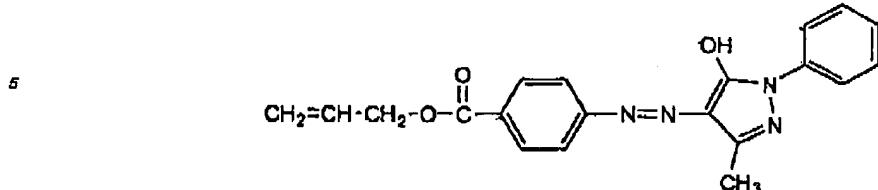
[0022] Examples of yellow dye embodying the present invention also have the above general formula [II] in addition to those having the above general formula

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[0023] Examples of such compounds are N,N-diallyl-4-aminoazobenzene, N-allyl-4-aminoazobenzene, 4-allyloxyethylazobenzene, N,N-dimethacryl-4-aminoazobenzene, N-methacryl-4-aminoazobenzene, 4-methacryloyloxyethylazobenzene, N,N-diallyl-4-(2-aminoethyl)azobenzene, N,N-diallyl-4-aminomethylazobenzene, N-allyl-4-(2-aminoethyl)azobenzene, N-allyl-4-aminomethylazobenzene, N,N-diethyl-4-amino-3-allylazobenzene, N,N-dimethyl-4-amino-3-allylazobenzene, N,N-diethyl-4-amino-4'-allylazobenzene, N,N-dimethyl-4-amino-4'-allylazobenzene and the like, but these are not limited to the above compounds.

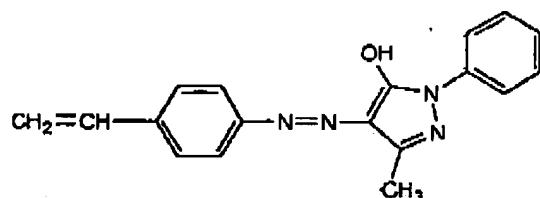
50 [0024] Preferred examples of dyes embodying the present invention are the following compounds 1, 2, 3 and 4.

EP 1 293 541 A2



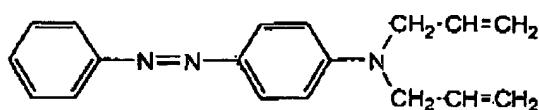
Compound 1

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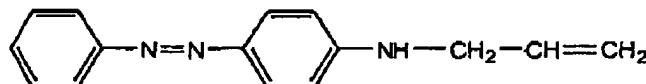
Compound 2

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Compound 3

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Compound 4

50 [0025] Compounds 1, 2, 3 and 4 have a possibility of covalent bonding of a silicone polymer, by an addition reaction of the end C=C bonds themselves with hydrosilyl groups of silicone having the hydrosilyl groups. Because of the reaction, dye exudates from such obtained materials are very little. Further it is possible to introduce these compounds into the polymer produced by radical polymerization.

55 [0026] The above dye compounds have a maximum absorbance of about 350-450nm. Some of them have a weak absorbance at less than 350nm. In such compounds, another ultraviolet absorbing agent should be preferably used at the same time. There are several types of ultraviolet absorbing agents, such as benzophenone, benzotriazole, salicylic acid and indole types, but such agents are not limited to these types. It is important that these types are used for compensating the absorbance of the above dyes and have functional groups which are able to chemically bind to

EP 1 293 541 A2

silicone to be main materials of lenses.

[0027] Examples of such ultraviolet absorbing agents are 2-(5-acryloyloxyethoxy-2-hydroxy-3-tert-butylphenyl)-2H-benzotriazole, 2-(2-hydroxy-5-acryloyloxyphenyl)-2H-benzotriazole, 2-(2-hydroxy-4-methacryloyloxyethoxy)-4-chloro-2H-benzotriazole, 2-(2-hydroxy-3-tert-butyl-5-vinylphenyl)-5-chloro-2H-benzotriazole, 2-(3-allyl-2-hydroxy-5-methylphenyl)-2H-benzotriazole, 2-(3-allyl-2-hydroxy-5-tert-butylphenyl)-2H-benzotriazole, 2-hydroxy-4-methacryloyloxybenzophenone, 2-hydroxy-4-methacryloyloxyethoxybenzophenone, 4-acryloyloxy-2-hydroxybenzophenone, 4-acryloyloxyethoxy-2-hydroxybenzophenone and the like, but these are not limited.

[0028] By using a yellow dye as an example of the present invention, having a possibility of addition reaction to silicone having hydroxyl groups, an addition reaction using a catalyst such as platinum can provide silicone compounds having a very low risk of elution of the dye directly bound to the silicone.

[0029] Examples of the above silicone compounds having hydroxyl groups are dimethylsiloxane-methylhydroxiloxane copolymer, diphenylsiloxane-phenylhydroxiloxane copolymer, polyethylhydroxiloxane, methylhydroxiloxane-phenylmethylsiloxane copolymer, methylhydroxiloxane-octylmethylsiloxane copolymer, methyl silicone resin containing hydroxyl groups, polyphenyl(dimethylhydroxiloxyl)siloxane and the like, but these are not limited to such compounds.

[0030] Catalysts using in the addition reaction of yellow dyes to silicone compounds are desirably platinum compounds such as hydrogen chloroplatinate, platinum-divinyltetramethyldisiloxane, and platinum-tetramethyltetravinylcyclotetrasiloxane. Further, a silicone bound to the yellow dye obtained by the above method may provide a silicone elastomer chemically bound to the yellow dye by crosslinking with a silicone having vinyl groups.

[0031] Further, a silicone bound to the above yellow dye may provide a silicone elastomer chemically bound to the yellow dye by crosslinking with a mixture of silicone having vinyl groups and silica.

[0032] To form the above elastomer, catalysts such as platinum compounds such as hydrogen chloroplatinate, a platinum-divinyltetramethyldisiloxane complex, a platinum tetramethyltetravinylcyclotetrasiloxane complex and a platinum-alumina supporting catalyst can be used, and such catalysts provide a smooth crosslinking reaction.

[0033] A yellow dye in accordance with one example of the present invention can be chemically bound to silicone having hydroxyl groups and then crosslinked with silicone having vinyl groups. Another method is that the yellow dye is mixed with silicone having hydroxyl groups or silicone having vinyl groups, and the mixture is mixed with silicone having hydroxyl groups and silicone having vinyl groups, and then the mixture is cross-linked at the same time as the yellow dye is reacted to the hydroxyl groups.

[0034] Upon mixing of the silicone described above, it is preferable to homogeneously disperse the yellow dye by using an appropriate solvent. As such solvents, acetone, ethanol, methanol, tetrahydrofuran, and dichloromethane can be exemplified. The yellow dye is dissolved in the solvent and mixed with silicone. Then, the solvent is distilled away with an evaporator, and the yellow dye can be uniformly dispersed in silicone.

35 Examples

[0035] The following are synthetic examples of compounds as used in examples of the present invention, and examples of use of such compounds.

40 Synthesis of compound 1

1. Synthesis of diazonium benzoate

[0036] *P*-amino benzoic acid 6.86 g (0.05 mol) was placed in a three-necked flask of 1000 ml, 1 mol/l of hydrochloric acid 100 ml was added to dissolve the mixture. A mechanical stirrer, a thermometer and a dropping funnel of 200ml were attached to the three-necked flask. The flask was placed in an ice bath, and the temperature in the flask was kept at 0-5°C. Sodium nitrite (NaNO₂) 8.8 g (0.055 mol) was dissolved in 10ml of distilled water, and the solution was slowly added dropwise from the neck into the flask for five minutes. The temperature in the flask was kept at 0-5°C, stirring was continued for 30 minutes, and yellow liquid was obtained to use for a subsequent reaction.

50 2. Synthesis of 4-(4'-carboxyphenylazo)-3-methyl-1-phenylpyrazolone by azo coupling reaction

[0037] 3-Methyl-1-phenylpyrazolone 10.45 g (0.06 mol) was dissolved in 1mol/l of aqueous solution of sodium hydroxide 100 ml and the solution was placed into the above dropping funnel. Vigorously stirring with a magnetic stirrer, the above aqueous solution was slowly added dropwise for one hour while it was kept at 0-5°C. After all the solution had been added, 1 mol/l of aqueous solution of sodium hydroxide 100ml was added, and the mixture was stirred for more two hours. After the reaction was finished, hydrochloric acid was added dropwise at room temperature, and 2N hydrochloric acid was slowly added dropwise to obtain a reaction solution of pH 2 with a monitor of pH test paper. A

EP 1 293 541 A2

large quantity of a precipitate was produced. The precipitate was filtered with Buchner funnel suction. The precipitate was washed with distilled water until the pH of the filtrate was 7. The suction was continued until no further filtrate was obtained, and the residue was washed with acetone 500 ml. The precipitate was placed in a heat dryer of 60°C and was dried under reduced pressure overnight with a vacuum pump.

5 3. Synthesis of 4-(4'-allyloxycarbonylphenylazo)-3-methyl-1-phenylpyrazolone

[0038] Dried solid 5g was collected from the above precipitate and placed in an oval flask of 300ml. Thionyl chloride 50ml was added, and a ball tipped cooler was attached to the flask. The flask was kept in an oil bath at 90°C ~ 100°C, and the mixture was reacted for 30 minutes. After the reaction was finished, thionyl chloride was distilled away under reduced pressure. Allyl alcohol 50 ml and pyridine 5 ml were added into the flask, and the mixture was stirred for 30 minutes at the oil bath temperature of 90-100°C and cooled to room temperature. The reaction solution was placed in a separating funnel of 1000 ml, and dichloromethane 100 ml and distilled water 100 ml were added. The solution was separated into two layers, and water of the upper layer and organic layer of the lower layer appeared. The lower organic layer was taken out of the funnel and washed with distilled water 100 ml, washed with 1 mol/l of aqueous solution of sodium hydroxide 100 ml three times, and washed with distilled water three times. It was confirmed with a pH test paper that the water layer had become neutral. The organic layer solution was taken out, after magnesium sulphate 5 g was added to the solution, the mixture was stirred for 3 minutes. Magnesium sulphate was filtered off without suction. Solvent was distilled away with an evaporator to obtain orange solid. The obtained solid was dissolved in methanol 200 ml and the mixture was submitted to heat filtration and cooled. Needle crystals separated out slowly and were left for about one hour in a refrigerator. The obtained needle crystals were separated by filtration, and dried in vacuo to obtain the crystals of the desired compound.

H-NMR: d=2.4, 4.8, 5.3-5.5, 6.0-6.1, 72-73, 74, 79, 8.1, 13.5ppm

1-T-IR: 3060, 1719, 1561, 1550, 1499, 1251, 1159, 1108, 765cm⁻¹

25 Synthesis of Compound 2

1. Synthesis of a diazonium salt of 4-aminostyrene

[0039] 1 N hydrochloric acid 100 ml was placed into a 1000ml three necked flask equipping with a thermometer, and 4-aminostyrene 2.5 g was added and dissolved. Ice cooling the flask, an aqueous solution 10 ml of sodium nitrite 1.45 g was slowly added for about ten minutes. All reaction solution was changed into green brown.

30 2. Synthesis of 3-methyl-1-phenyl-4-(4-vinylphenylazo)-5-pyrazolone by azo coupling reaction

[0040] 3-methyl-1-phenylpyrazolone 3.7 g was dissolved in 1 N aqueous solution 200 ml of sodium hydroxide. The solution was placed in a dropping funnel, and slowly added dropwise for about one hour into the solution prepared in 1 above. With dropping, a red brown precipitate was produced in the solution. After the dropping was finished, the solution was warmed to room temperature, and stirred for one hour. Measuring with a pH meter, 1 N hydrochloric acid was added to obtain a solution of pH 2. The solution was filtered with suction, and the precipitate was obtained. The precipitate was washed well with water, and dried in vacuo overnight.

35 3. Preparation of 3-methyl-1-phenyl-4-(4-vinylphenylazo)-5-pyrazolone

[0041] Toluene 100 ml was added into the solid obtained in 2 above, and the mixture was heated to 70-80°C and dissolved. The mixture was filtered without suction with filter paper to filter off impurities. After removing toluene with an evaporator, the residue was dried and recrystallized from small amounts of methanol to obtain needle crystals of the desired compound.

H-NMR: d=2.4, 5.3, 5.7, 6.7, 7.2-7.3, 7.4-7.5, 8.0, 13.7ppm

40 FT-IR: 3060, 3006, 2921, 1654, 1582, 1550, 1501, 1490, 1341, 1270, 1155, 994, 913, 753cm⁻¹

Synthesis of Compound 3

[0042] 4-aminoazobenzene 1 g was dissolved in a mixture of ethanol 40 ml and toluene 5 ml in an oval flask of 200 ml, and allyl bromide 10 ml was added. The flask was immersed in an oil bath at 80°C and heated to reflux the mixture for 30 minutes. Then, by adding NaOH 2 g, the colour of the solution was changed into greenish yellow. Allyl bromide 10 ml was further added, and the mixture was refluxed at 80°C for 30 minutes. After the reaction was finished, dichloromethane 100 ml was added, and the solution was washed with 1N NaOH aqueous solution three times and water

EP 1 293 541 A2

100 ml three times. The dichloromethane layer was taken out and the solvent was distilled away with an evaporator. After adding a small amount of ethanol, the mixture was submitted to heat filtration and cooled in a refrigerator. Needles crystals separated out. The obtained crystals were filtered and dried in vacuo to obtain crystals of the desired compound. [0043] Further examples of the invention are as follows.

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Example 1: Production of coloured silicone with compound 1

[0044] Compound 1 0.01g, 2-hydroxy-4-methacryloyloxyethoxybenzophenone 0.5g commercially available as an ultraviolet absorber, and KE-103 100g (manufactured by Shinetsu Silicone, principal constituent: vinyl-terminated polydimethylsiloxane) which is a transparent silicone of a two-part hard type commercially available as a principal material, these three compounds were mixed with stirring to uniformly distribute compound 1 and the ultraviolet absorber. To the resulting principal material of silicone in which compound 1 and the ultraviolet absorber were uniformly dispersed, CAT-103, which is a silicone-crosslinking agent attached to KE-103, was mixed in the weight ratio of 1/10 per silicone. After removing bubbles by vacuum degassing, the mixture was interposed with glass plates and heat cross-linked at 100°C for 30 minutes to obtain a plate sample of a coloured silicone elastomer. Figure 1 shows a transmittance spectrum of the ultraviolet-visible light of the plate sample.

Example 2: Production of coloured acrylic resin with compound 2

[0045] The following materials were mixed: compound 2 0.01% by weight, phenylethylacrylate 60% by weight, phenylethylmethacrylate 34% by weight, 1,3-propanedioldiacrylate 3.5% by weight, 2-(2-hydroxy-5-acryloyloxyphenyl)-2H-benzotriazol 1.5% by weight, AIBN 1% by weight as an initiator. The mixture was interposed between glass plates and polymerized at 100 °C for 2 hours. After extracting unreacted materials from the polymer with acetone by a Soxhlet's extractor, the polymer was dried in vacuo to obtain an acrylic plate sample.

Example 3: Production of coloured silicone with compound 3

[0046] To 100 g of commercially available trimethylsilyl-terminated dimethylsiloxane-methylhydrosiloxane copolymer (Aldrich) which was heated to 90 °C, 0.1 g of compound 3 and 5 g of 2-hydroxy-4-methacryloyloxyethoxybenzophenone was added, and a commercial complex of platinum-divinyltetramethyldisiloxane (Aldrich) was added to obtain platinum concentration of 5 ppm. The mixture was reacted at 80 °C for one hour. After cooling the reactant, filtration was conducted with a 0.5μ membrane filter to obtain an orange silicone cross-linking agent. The coloured silicone cross-linking agent was mixed with KE-103 (manufactured by Shinetsu silicone, principal constituent : vinyl-terminated polydimethylsiloxane) in the ratio of 1/10 per the principal material. After removing bubbles by vacuum degassing, the mixture was interposed with glass plates and heat cross-linked at 100 °C for 30 minutes to obtain a plate sample of a coloured silicone. Figure 2 shows a transmittance spectrum of the ultraviolet-visible light of the plate sample.

Comparative Example 1:

[0047] C.I.Solvent Yellow 16 of a commercial dye 0.01 g, 2-hydroxy-4-methacryloyloxyethoxybenzophenone of a commercial polymerizable ultraviolet absorber 0.1 g, and a transparent silicone 100 g of a commercial two-part hard type as a principal material were mixed with stirring to distribute uniformly the dye and the ultraviolet absorber. The resulting principal material of coloured silicone and a usual silicone cross-linking agent were mixed with a suitable mixing ratio. The mixture was interposed between glass plates and heat cross-linked to obtain a plate sample of a coloured silicone elastomer. Since the thus-obtained coloured silicone elastomer easily exuded the dye on the surface, it was not appropriate for use as a material in contact with living organisms.

[0048] In this specification, the verb "comprise" has its normal dictionary meaning, to denote non-exclusive inclusion. That is, use of the word "comprise" (or any of its derivatives) to include one feature or more, does not exclude the possibility of also including further features.

[0049] The reader's attention is directed to all and any priority documents identified in connection with this application and to all and any papers and documents which are filed concurrently with or previous to this specification in connection with this application and which are open to public inspection with this specification, and the contents of all such papers and documents are incorporated herein by reference.

[0050] All of the features disclosed in this specification (including any accompanying claims, abstract and drawings), and/or all of the steps of any method or process so disclosed, may be combined in any combination, except combinations where at least some of such features and/or steps are mutually exclusive.

[0051] Each feature disclosed in this specification (including any accompanying claims, abstract and drawings), may be replaced by alternative features serving the same, equivalent or similar purpose, unless expressly stated otherwise.

EP 1 293 541 A2

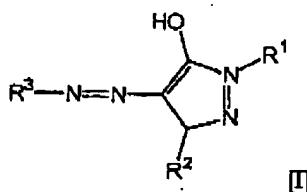
Thus, unless expressly stated otherwise, each feature disclosed is one example only of a generic series of equivalent or similar features.

[0052] The invention is not restricted to the details of the foregoing embodiment(s). The invention extends to any novel one, or any novel combination, of the features disclosed in this specification (including any accompanying claims, abstract and drawings), or to any novel one, or any novel combination, of the steps of any method or process so disclosed.

Claims

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1. A dye for an intraocular lens having the following formula [I] or [II]:

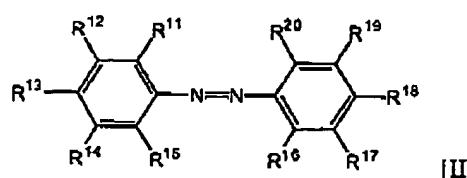


wherein R¹ is linear or branched alkyl of C₁-C₁₀ or phenyl; when R¹ is phenyl, one or more hydrogens of its aromatic ring may be substituted by linear or branched alkyl of C₁-C₁₀, linear or branched alkoxy of C₁-C₁₀, hydroxy, amino, sulfo, nitro, halogen, carboxy, -C(=O)-O-R⁴ or -C(=O)-NH-R⁴, wherein R⁴ is linear or branched alkyl of C₁-C₁₀;

R² is linear or branched alkyl of C₁-C₁₀, amino or phenyl; when R² is amino, one or both hydrogens thereof may be substituted by linear or branched alkyl of C₁-C₁₀; or when R² is phenyl, one or more hydrogens of its aromatic ring may be substituted by linear or branched alkyl of C₁-C₁₀, linear or branched alkoxy of C₁-C₁₀, hydroxy, amino, sulfo, nitro, halogen, carboxy, -C(=O)-O-R⁴, -C(=O)-NH-R⁴, wherein R⁴ is linear or branched alkyl of C₁-C₁₀;

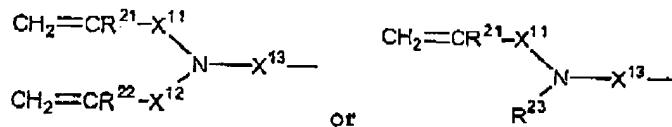
R³ is phenyl or naphthyl, one or more hydrogens thereof are linear or branched alkyl of C₁-C₁₀, linear or branched alkoxy of C₁-C₁₀, hydroxy, amino, sulfo, nitro, halogen, carboxy, -C(=O)-O-R⁴, -C(=O)-NH-R⁴, wherein R⁴ is linear or branched alkyl of C₁-C₁₀; and

in formula [II], at least one hydrogen of the aromatic ring constituted in R¹, R² or R³ is substituted by any of CH₂=CH-(CH₂)_m, CH₂=CH-(CH₂)_m-X¹-(CH₂)_n, CH₂=C(R⁵)-(CH₂)_m-X¹-C(=O)-(CH₂)_n, CH₂=C(R⁵)-(CH₂)_m-C(=O)-X¹-(CH₂)_n, (CH₂=C(R⁵)-(CH₂)_m)₂N-(CH₂)_n, or (CH₂=C(R⁵)-(CH₂)_m)₂N-C(=O)-(CH₂)_n; wherein X¹ is -O- or -NR⁶, R⁵ and R⁶ are independently hydrogen, or linear or branched alkyl of C₁-C₁₀, and m and n are independently integers in the range 0 to 10:



wherein R¹¹, R¹², R¹³, R¹⁴, R¹⁵, R¹⁶, R¹⁷, R¹⁸, R¹⁹, and R²⁰ are independently selected from hydrogen, hydroxy, halogen, or linear or branched alkyl of C₁-C₁₀, and at least one of them is a substituted group represented by:

EP 1 293 541 A2



10 wherein R²¹ and R²² are independently hydrogen or methyl, R²³ is hydrogen or linear or branched alkyl of C₁–C₁₀, X¹¹, X¹² and X¹³, independently, have covalent bonds, or linear or branched bivalent spacer groups, or -(CH₂)_m-O-(CH₂)_n-, wherein m and n are independently integers in the range 0 to 10.

15 2. A colouring silicone material which is obtained from chemical bonding of the dye represented by formula [I] or [II] of claim 1 to a silicone polymer having hydrosilyl groups.

20 3. A colouring silicone material which is obtained from chemical bonding of the dye represented by formula [I] or [II] of claim 1 and an ultraviolet absorber having functional groups capable of chemical bonding to a silicone having hydrosilyl groups.

25 4. A colouring silicone material according to claim 2 or 3, in which the silicone having hydrosilyl groups is selected from the group comprising a dimethylsiloxane-methylhydrosiloxane copolymer, a diphenylsiloxane-phenylhydrosiloxane copolymer, polyethylhydrosiloxane, a methylhydrosiloxane-phenylmethylsiloxane copolymer, a methylhydrosiloxane-octylmethylsiloxane copolymer, a silicone resin containing hydrosilyl groups and polyphenyl(dimethylhydrosiloxyl)siloxane.

30 5. A silicone elastomer obtained by crosslinking of a silicone having hydrosilyl groups according to claim 2 or 3 with a silicone having vinyl groups.

6. A silicone elastomer obtained by crosslinking of a silicone having hydrosilyl groups according to claim 2 or 3 with a silicone having vinyl groups and a silica.

35 7. An intraocular lens comprising a dye, colouring silicone material or silicone elastomer as claimed in any of the preceding claims.

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EP 1 293 541 A2

FIG. 1

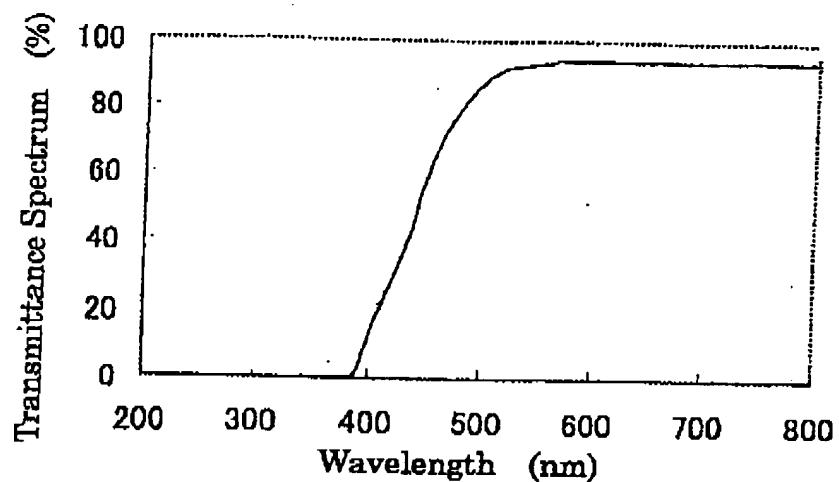
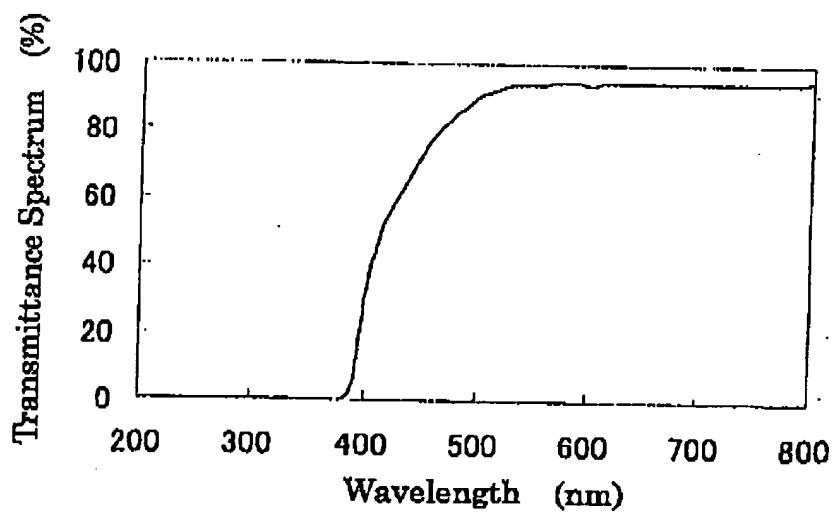
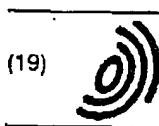


FIG. 2





(19)

Europäisches Patentamt

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EP 1 293 541 A3

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(54) Intraocular lens and dye therefor

(57) A yellow dye is capable of chemical bonding to a silicone which is a material of an intraocular lens or capable of copolymerizing with a radical polymerizable monomer which is a material of an intraocular lens. Such a dye is useful for providing lenses for eyes, having vis-

ible light transmission properties near to those of human crystalline lenses, and may be particularly effective for soft lenses for eyes.

EP 1 293 541 A3

EP 1 293 541 A3

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EUROPEAN SEARCH REPORT

Application Number

EP 02 25 6409

DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (IPC67)						
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim							
X	<p>DATABASE WPI Section Ch, Week 200027 Derwent Publications Ltd., London, GB; Class A26, AN 2000-308085 XP002227200 -& JP 2000 089171 A (CANONSTAR KK), 31 March 2000 (2000-03-31) * abstract *</p> <p>—</p> <p>DATABASE CA 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; SINYAVSKII, V. G. ET AL: "Synthesis of p-aminostyrene, azomethines, and azo dyes containing the vinyl group" retrieved from STN Database accession no. 65:47377 XP002227199 * abstract * & UKR. KHIM. ZH. (1966), 32(5), 489-93,</p> <p>—</p> <p>GB 1 269 627 A (IMPERIAL CHEMICAL INDUSTRIES LTD.) 6 April 1972 (1972-04-05) * examples 3,4 *</p> <p>—</p> <p>—/—</p>	1-7	C09B69/10 A61L27/18 G02B1/04						
X		1							
X		1							
			TECHNICAL FIELDS SEARCHED (IPC67)						
			A61L C09B G02B						
<p>The present search report has been drawn up for all claims</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 33%;">Place of search</td> <td style="width: 33%;">Date of completion of the search</td> <td style="width: 34%;">Examiner</td> </tr> <tr> <td>THE HAGUE</td> <td>25 March 2003</td> <td>Muñoz, M</td> </tr> </table> <p>CATEGORY OF CITED DOCUMENTS</p> <p>X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background D : non-written disclosure P : Informative document</p> <p>T : theory or principle underlying the invention E : earlier patent document, but published on, or, after the filing date D : document cited in the Application L : document cited for other reasons S : member of the same patent family, corresponding document</p>				Place of search	Date of completion of the search	Examiner	THE HAGUE	25 March 2003	Muñoz, M
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EP 1 293 541 A3

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DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (MCL/7)
X	<p>DATABASE CA 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US;</p> <p>ENDO, HIDEO ET. AL: "Growth-inhibitory activity of allyl-substituted compounds against sarcoma 180 and carcinoma 63 in mice"</p> <p>retrieved from STN</p> <p>Database accession no. 60:18986</p> <p>XP002235868</p> <p>* abstract *</p> <p>& SCI. REPT. RES. INST., TOHOKU UNIV. SER. C (1963), 11(2), 187-91,</p>	1	
A,D	<p>US 5 470 932 A (JINKERSON DAVID L)</p> <p>28 November 1995 (1995-11-28)</p> <p>* column 7, line 1 - line 10 +</p>	1-7	
The present search report has been drawn up for all claims			
Place of search	Date of completion of the search	Examiner	
THE HAGUE	25 March 2003	Muñoz, M	
CATEGORY OF CITED DOCUMENTS X: particularly relevant if taken alone Y: particularly relevant if combined with another document of the same category A: technological background D: non-written disclosure P: intermediate document T: theory or principle underlying the invention E: earlier patent document, but published on or after the filing date D: document cited in the application L: document cited for other reasons &: member of the same patent family, corresponding document			

EP 1 293 541 A3

European Patent
Office

Application Number

EP 02 25 6409

CLAIMS INCURRING FEES

The present European patent application comprised at the time of filing more than ten claims.

- Only part of the claims have been paid within the prescribed time limit. The present European search report has been drawn up for the first ten claims and for those claims for which claims fees have been paid, namely claim(s):

- No claims fees have been paid within the prescribed time limit. The present European search report has been drawn up for the first ten claims.

LACK OF UNITY OF INVENTION

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

see sheet B

- All further search fees have been paid within the fixed time limit. The present European search report has been drawn up for all claims.

- As all searchable claims could be searched without effort justifying an additional fee, the Search Division did not invite payment of any additional fee.

- Only part of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the inventions in respect of which search fees have been paid, namely claims:

- None of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims, namely claims:

EP 1 293 541 A3

European Patent
OfficeLACK OF UNITY OF INVENTION
SHEET 8

Application Number

EP 02 25 6409

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

1. Claims: 1-7 (in part)

Dyes for intraocular lenses of formula 'I', silicone material containing said dye and intraocular lens comprising said silicon material.

2. Claims: 1-7 (in part)

Dyes for intraocular lenses of formula 'III', silicone material containing said dye and intraocular lens comprising said silicon material.

EP 1 293 541 A3

**ANNEX TO THE EUROPEAN SEARCH REPORT
ON EUROPEAN PATENT APPLICATION NO.**

EP 02 25 6409

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EPO file on The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

25-03-2003

For more details about this annex ; see Official Journal of the European Patent Office, No. 12/82